



BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. to achieve expeditious commercialization of results of federally-funded research and development.

FOR FURTHER INFORMATION CONTACT: Licensing information may be obtained by emailing the indicated licensing contact at the National Heart, Lung, and Blood, Office of Technology Transfer and Development Office of Technology Transfer, 31 Center Drive Room 4A29, MSC2479, Bethesda, MD 20892-2479; telephone: 301-402-5579. A signed Confidential Disclosure Agreement may be required to receive any unpublished information.

SUPPLEMENTARY INFORMATION: Technology description follows.

High Density Lipoprotein (HDL) Targeting Protease Inhibitor

Available for licensing and commercial development is intellectual property covering a class of lipoproteins targeting protease inhibitors and methods of their use for treating a protease-mediated disease. Alpha-1-antitrypsin (A1AT) deficiency occurs in about 1 in 2500 individuals in the United States and Europe. Persons with this condition develop severe liver disease and emphysema/chronic obstructive pulmonary disease (COPD). The

current treatment for A1AT deficiency includes intravenous infusion of purified human A1AT protein. This treatment strategy is expensive and only moderately effective. A recent study demonstrated improvement in the treatment of A1AT deficiency in a mouse model of emphysema by pre-incubating A1AT with high density lipoprotein (HDL) particles prior to infusion. This resulted in improvements in lung morphology and inflammatory markers in the lung compared to A1AT treatment alone. The mechanism for this improvement in function of A1AT when bound to HDL is believed to be increased trafficking of A1AT to the lung. The lipoprotein targeting protease inhibitory peptide of the present invention represents provides advances upon these existing methods. First, it replaces the need for full length A1AT protein with a known small peptide inhibitor of elastase (the natural target protease of A1AT; a small tetra-peptide with the sequence Ala-Ala-Pro-Val-chloromethylketone). Second, the peptide can be conjugated by amine reactive chemistry to a lipoprotein targeting motif. The inventors have data linking the peptide to a Vitamin E with a polyethylene glycol spacer arm to distance the functional AAPV peptide from the targeting moiety and to provide improved solubility. Third, the approach promises improved efficacy over the current standard of care (A1AT infusion) because the overall molecule is small molecule, 2.5 kDa versus 52 kDa for the the full length A1AT protein. An HDL particle can generally accommodate only one molecule of A1AT, whereas many copies of our VitE-PEG-AAPV peptide can reside on an HDL particle providing a significant increase in potency.

Potential Commercial Applications:

- Alpha-1-antitrypsin deficiency
- severe liver disease

- emphysema/chronic obstructive pulmonary disease

Development Stage:

- Early stage

Inventors: Alan Remaley and Scott Maxwell Gordon (both of NHLBI)

Relevant Publications: Gordon, et al. Molecular & Cellular Proteomics 14: 10.1074/ mcp.M115.054031, 3247–3257, 2015.

Intellectual Property: HHS Reference No. E-155-2016; U.S Patent Application 15/297,054 filed October 18, 2016.

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Dated: September 24, 2018.

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